

PRODUCT INFORMATION



Siremadlin

Item No. 38516

CAS Registry No.: 1448867-41-1
Formal Name: (6S)-5-(5-chloro-1,2-dihydro-1-methyl-2-oxo-3-pyridinyl)-6-(4-chlorophenyl)-2-(2,4-dimethoxy-5-pyrimidinyl)-5,6-dihydro-1-(1-methylethyl)-pyrrolo-[3,4-d]imidazol-4(1H)-one

Synonyms: HDM201, NVP-HDM201

MF: C₂₆H₂₄Cl₂N₆O₄

FW: 555.4

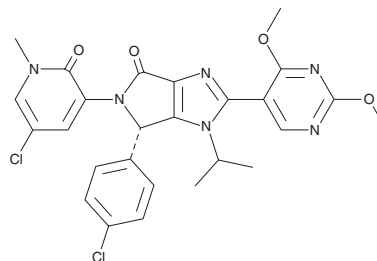
Purity: ≥98%

UV/Vis.: λ_{max}: 223, 336 nm

Supplied as: A solid

Storage: -20°C

Stability: ≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

Siremadlin is supplied as a solid. A stock solution may be made by dissolving the siremadlin in the solvent of choice, which should be purged with an inert gas. Siremadlin is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of siremadlin in these solvents is approximately 15, 10, and 20 mg/ml, respectively.

Description

Siremadlin is an inhibitor of the protein-protein interaction between the E3 ubiquitin ligase MDM2 and p53 (IC₅₀ = 0.21 nM).¹ It selectively inhibits the MDM2-p53 protein-protein interaction over MDM4-p53, YAP1-TEAD4, PCSK9-LDLR, and Bcl-2-Bak interactions in time-resolved FRET (TR-FRET) assays (IC₅₀s = 3.3, >150, >50, and >50 μM, respectively). Siremadlin inhibits the growth of SJSA-1 osteosarcoma cells (GI₅₀ = 38 nM). It also induces apoptosis in SJSA-1 cells when used at a concentration of 100 nM. *In vivo*, siremadlin (27 mg/kg) induces tumor regression and prevents tumor regrowth in an SJSA-1 rat xenograft model and an HSAX2655 patient-derived xenograft (PDX) rat liposarcoma model.

Reference

1. Jeay, S., Ferretti, S., Holzer, P., *et al.* Dose and schedule determine distinct molecular mechanisms underlying the efficacy of the p53-MDM2 inhibitor HDM201. *Cancer Res.* **78(21)**, 6257-6267 (2018).

WARNING

THIS PRODUCT IS FOR RESEARCH ONLY - NOT FOR HUMAN OR VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

SAFETY DATA

This material should be considered hazardous until further information becomes available. Do not ingest, inhale, get in eyes, on skin, or on clothing. Wash thoroughly after handling. Before use, the user must review the complete Safety Data Sheet, which has been sent via email to your institution.

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